SCANCELL

A NEW FRONTIER IN T-CELL ACTIVATION AND TARGETING

AGM PRESENTATION
October 10th 2017

Dr John Chiplin: Executive Chairman
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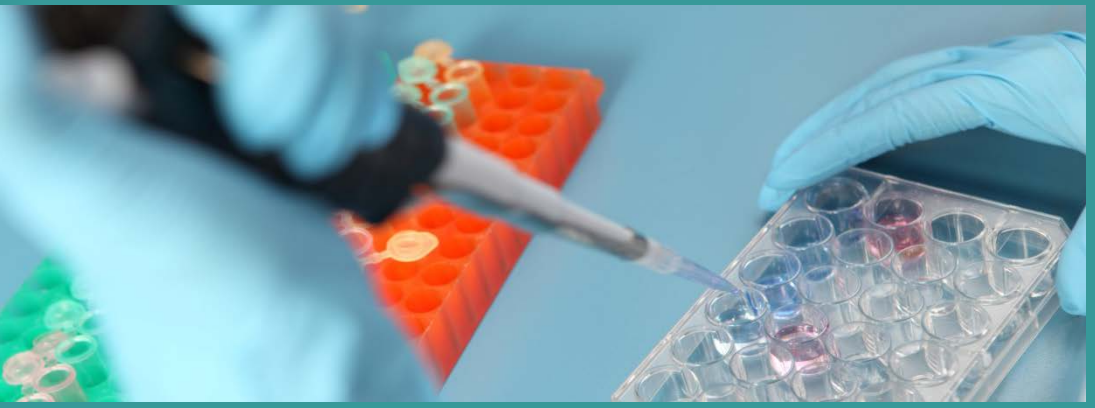

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BROAD IMMUNO-ONCOLOGY PIPELINE

2 PLATFORMS, 3 PRODUCTS, 5 CANCER INDICATIONS

- **Two** disruptive immuno-oncology platforms delivering potent killer T cells without serious side effects
- **Three** lead products addressing **five** high value disease areas
- Moditope® platform overcomes immunosuppression and delivers potent killer T cell responses that destroy cancer in animals – lead product Modi-1 targeting breast cancer, ovarian cancer and sarcoma initially
- Lead ImmunoBody® product SCIB1 offers potentially curative potential in resected stage III/IV melanoma patients with survival "well beyond established norms", mostly without disease progression
- Second ImmunoBody® SCIB2 defined and focused on NSCLC in combination with checkpoint inhibition

STRONG PROGRESS ON ALL FRONTS

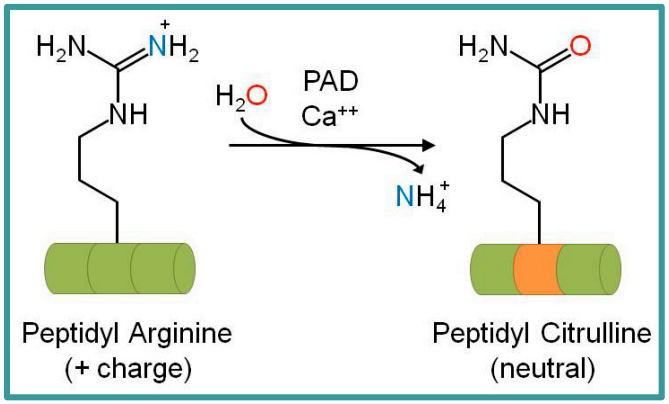
- Landmark 5-year survival achieved in resected SCIB1 melanoma patients (90% survival including seven patients alive after 5 years)
- Production and release of new GMP batch of SCIB1 successfully completed with gold-standard manufacturer
- IND application for SCIB1 Phase 2 checkpoint inhibitor (CPI) combination trial in US to be submitted early 2018
- SCIB2 ready to be developed in NSCLC in combination with a CPI
- Ultra-efficient linked adjuvant identified for Modi-1 increasing potency up to 100-fold; process development for manufacture underway
- Patent granted in Europe for Scancell's platform DNA ImmunoBody® technology (in addition to US and Japan)
- Very broad IP protection for use of citrullinated peptides (Moditope®) for the treatment of cancer likely
- £5m raised in May to support continued Moditope® development
- Multiple partnering and funding discussions in progress
- New Head Office established in Oxford, UK
- New CEO identified, starting January 2018

THE MODITOPE® PLATFORM

A NOVEL IMMUNOTHERAPY THAT OVERCOMES IMMUNOSUPPRESSION AND DELIVERS UNPRECEDENTED KILLER T-HELPER CELL RESPONSES

- Post-translational modifications of proteins occur under conditions of cellular stress
- One such modification involves the process of **CITRULLINATION**

  - *Involves the alteration of proteins due to enzymatic conversion of arginine residues to citrulline*
  - *Citrullination occurs as a result of a degradation and 'recycling' process called **autophagy** that is induced in stressed cells, including cancer cells*
  - *Citrullinated epitopes presented on MHC class II*



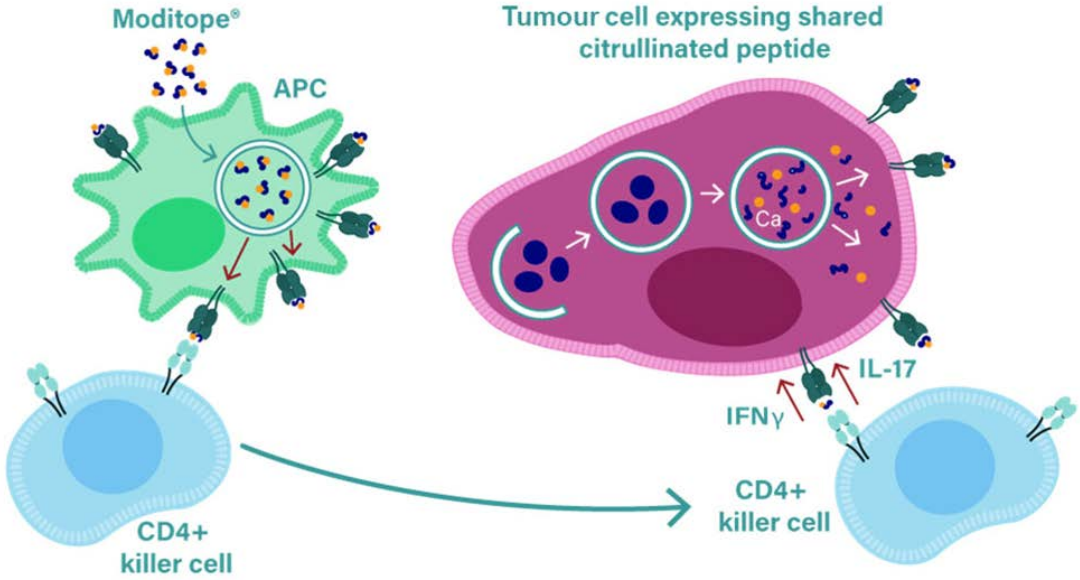
PAD = peptidylarginine deiminase

- The Moditope® platform is based on exploiting this normal immune response to stressed cells, which is largely mediated by cytotoxic CD4 T cells
- The novelty of the technology is harnessing this mechanism to eradicate tumour cells by immunizing with citrullinated peptides

MODE OF ACTION

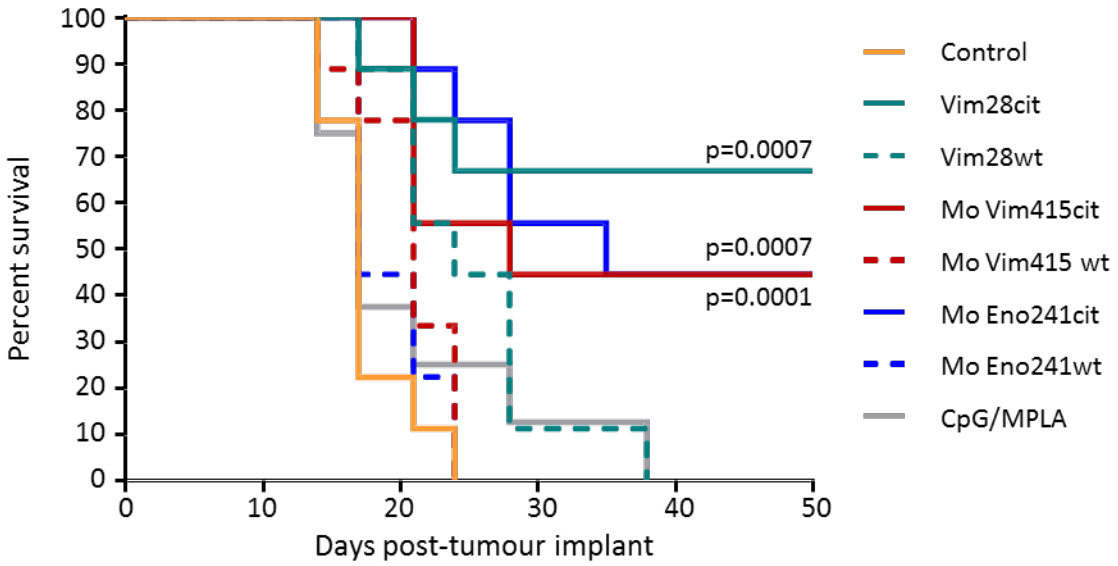
CITRULLINATED PEPTIDES (MODITOPE®) ACTIVATE KILLER T-HELPER CELLS THAT SEEK AND DESTROY CANCER CELLS

- Citrullinated tumour-associated peptides (Moditope peptides) are administered with adjuvant to activate antigen presenting cells (APCs)
- Moditope peptides are taken up by activated APCs
- APCs present peptides to CD4⁺ killer T-cells
- Primed CD4⁺ killer T-cells enter the circulation
- Stressed tumour cells undergo autophagy and produce citrullinated peptides
- CD4 T cell release IFNγ at the tumour site and induce expression of MHC-II expressing the citrullinated epitopes
- Primed CD4⁺ killer T-cells destroy cancer cells

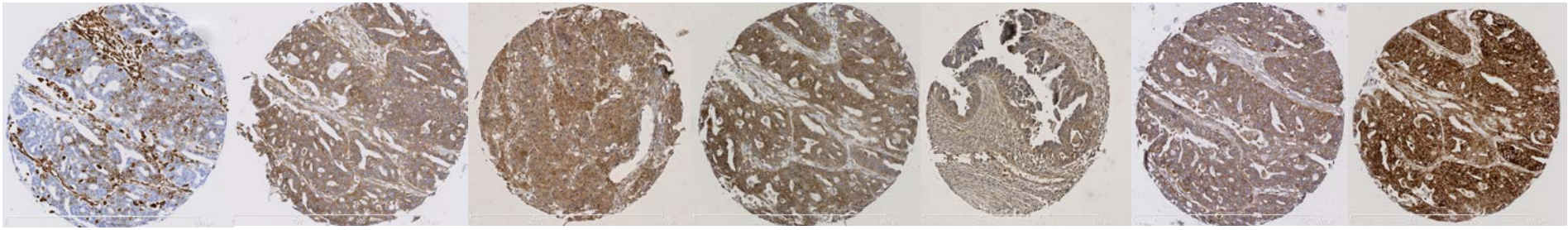


WILD-TYPE PEPTIDES DO NOT INDUCE AN ANTI-TUMOUR RESPONSE

- Citrullinated vimentin and enolase peptides induced high levels of IFNγ-secreting T cell responses in mice
- Potent anti-tumour responses induced in mice with established melanoma (B16 iDR4, iDP4), ovarian (ID8-DP4), pancreatic (Pan02-DR4) and lung (LLC4-DR4) tumours
- Wild type peptides do not induce an anti-tumour response as they are cleaved by proteases thus minimizing toxicity



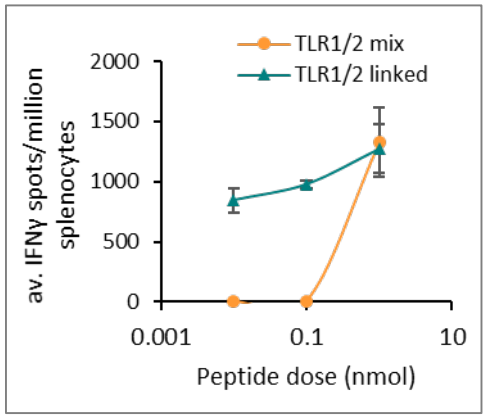
MODI-1



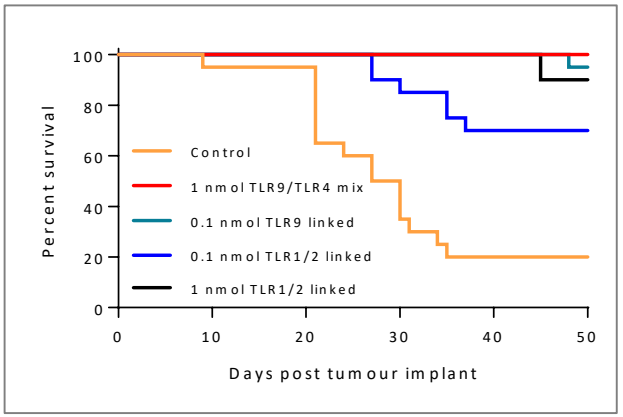
Vimentin | Citrullinated vimentin | Enolase | PAD2 | PAD4 | Ambra-autophagy | P62 autophagy

- Vimentin and/or enolase targets, PADs and autophagy are highly expressed in triple negative breast cancer (90%), ovarian cancer (95%), renal cancer and sarcoma (100%)
- Citrullinated vimentin is highly expressed
- Monoclonal antibody to citrullinated enolase was not specific so developing mass spectroscopy protocols
- Linked adjuvant allows a 10-100 fold reduction in dose
- Modi-1 induces memory responses which will prevent recurrence

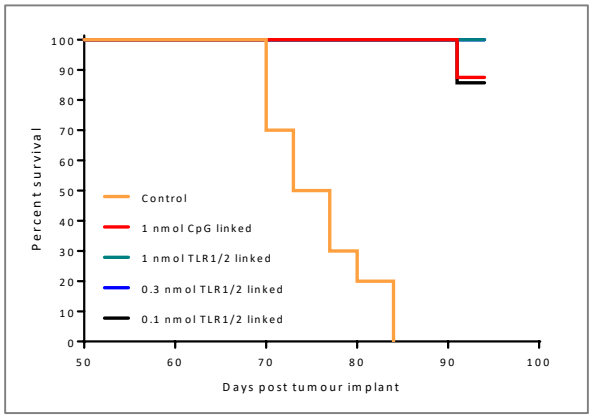
T cell response



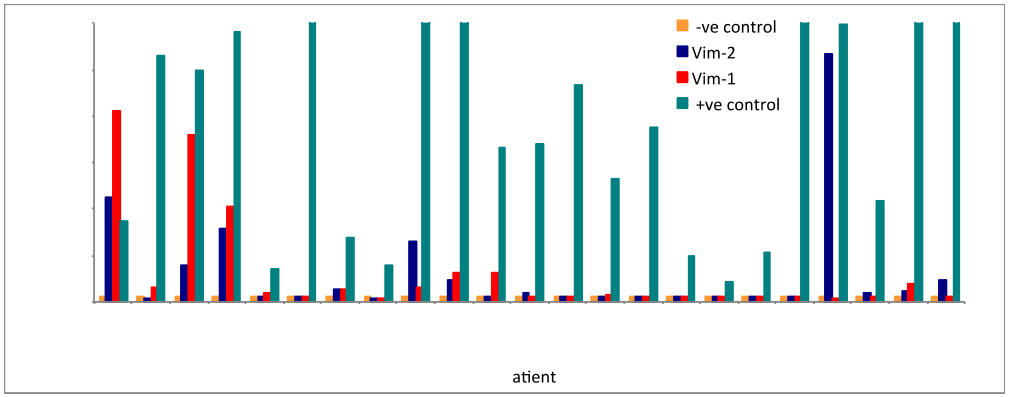
Survival



Rechallenge (survival)

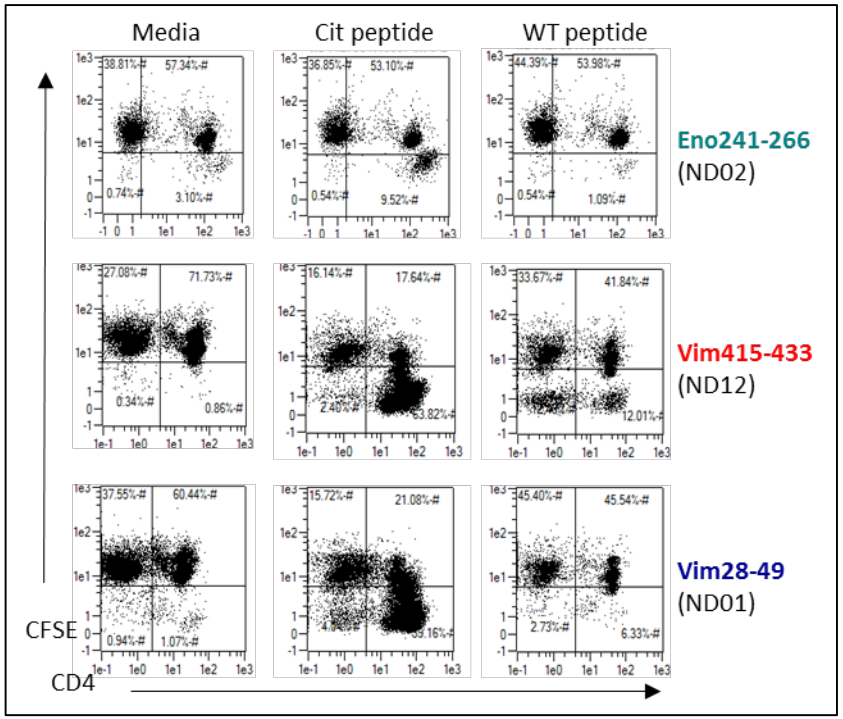


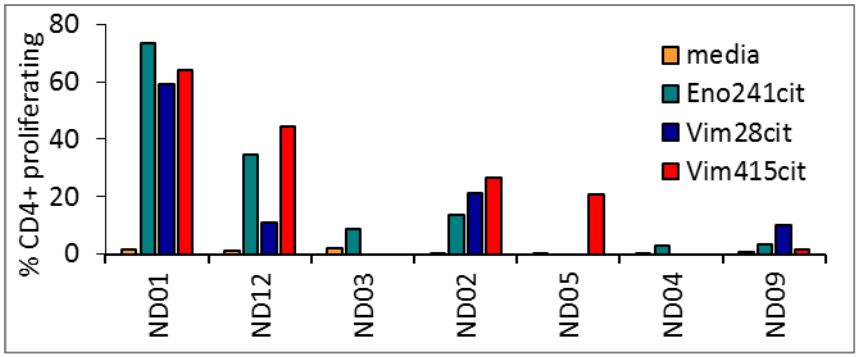
MODITOPE® RESPONSES IN CANCER PATIENTS & NORMAL DONORS



Samples from cancer patients tested in proliferation assay against citrullinated peptides

- 8/23 patients respond to Vim415cit (Vim-1)
- 8/23 patients respond to to Vim28cit (Vim-2)
- 5/23 patients respond to both Vim415cit and Vim28cit

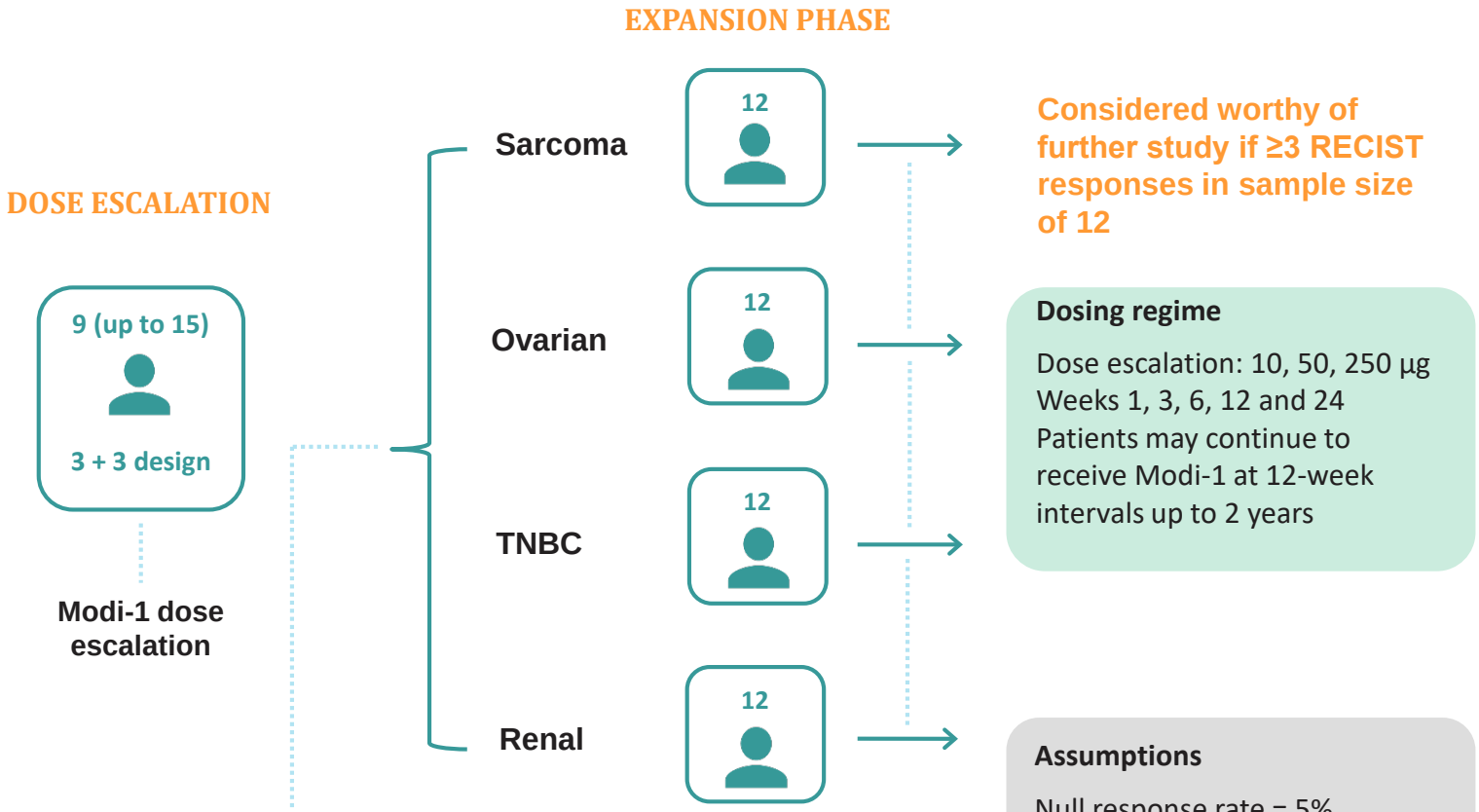




Samples from normal donors tested in CFSE proliferation assay against wild type and citrullinated peptides

- All 7 donors responded to one or more epitopes
- These assays will be used to monitor patients in the proposed clinical study

MODI-1 PHASE 1/2 CLINICAL TRIAL



HEALTHCARE CHALLENGE

TREATMENT OF ADVANCED, SOLID TUMOURS WHERE UNMET MEDICAL NEED FOR IMPROVED THERAPIES PERSISTS

- High mortality rate associated with cancer remains despite introduction of checkpoint inhibitors (CPI)
- 'Hot' tumours with dense T cell infiltrate respond to CPI better than 'cold' tumours with little or no T cell infiltrate
- Modi-1 aims to treat these large, bulky 'cold' tumours that do not respond to other therapies
- Sarcomas: relatively rare, not extensively studied, 5-year survival rate is only 16%
- Ovarian cancer: one of most common cancers in women, very hard to cure with standard approaches, tumours that recur after remission are usually resistant to further chemotherapy
- TNBC: accounts for 15-20% of all breast cancers (the most common cancer in the UK), heterogeneous disease, occurs most frequently in younger women and is characterised by rapid growth and metastases
- Renal cancer: 7th most common cancer in UK, 5-year survival only 12% for patients with distant metastases, still a need for more active therapies with acceptable side effect profiles

PATENTS

- European patent for citrullinated peptides for treatment of cancer about to be awarded
  - Divisional filed for nucleic acid vaccines
  - Divisional filed for the use of Moditope® T cell receptors for adoptive T cell therapy
- Patents in other jurisdictions being examined
- Patent filed on citrullinated enolase peptides for the treatment of cancer
- Patent licensed from Curara for citrullinated enolase peptide
- Patents being written for new citrullinated epitopes
- Patents being written for new modification
- Patents being written for new combinations

SUMMARY

- Moditope induces potent CD4 T cell responses that do not require CD8 T cells or checkpoint blockade to mount strong anti-tumour responses in bulky tumours
- Lead product Modi-1 (three citrullinated peptides linked to a potent and novel adjuvant) defined and ready for further development
- Five new Moditope® epitopes expressed by common solid tumours have been identified
- A new modification has been validated
- Patent family being awarded and extended
- New approaches being explored

Thank you